REMARKS

Claims 85-92 and 107-111 are pending and stand rejected. Claims 85, 87, 90, 107, and 109-111 have been amended. Support for the amendments can be found, for example, in the original claims, Figures 1-3, and paragraphs 009, 0013, 0060-0062, 0110-0119 and 0078-0091. Applicants note that some of the amendments merely rearrange the positioning of the elements in the claims. No new matter has been added by these amendments.

Applicants appreciate the opportunity to discuss the presently claimed method with the Examiner on September 22, 2006 and October 12, 2006. Applicants have amended the claims in line with the proposed modifications that were generally discussed in the interviews. As noted in the interview summary, the amendments clarify and further distinguish the cited art.

The claims are sufficiently clear as currently proposed.

As noted in the Interview Summary, Applicants agreed to amend the claims to address some possible confusion that could have resulted from the incorporation of a previous dependent claim into the independent claims as the Examiner noted in the rejection under 35 U.S.C. § 112. Applicants submit that the current amendment resolves this issue in making it clear that the scaling of the affinities is an active step. In light of this, Applicants request that the rejection under 35 U.S.C. §112 be withdrawn and the claims allowed.

The claims are novel and non-obvious over Rognan alone or in combination with Meister and Altuvia.

Previously pending Claims 85-89, 107, and 108 were rejected as anticipated by Rognan et al. The claims have been amended to further emphasize the differences between the teachings of Rognan et al. and the presently claimed method. Applicants note that Rognan et al. is discussed in the current application (see, *e.g.*, 0008 and 0056-0058 of the published application) which notes that Rognan is a "structure" based prediction method that relies upon determining binding energies to determine a single final prediction. In contrast, the present claims are directed to a method that would be applied primarily after the method described in Rognan. That is, the result of the Rognan method could be used in the claimed methods (as one prediction), but the Rognan method does not anticipate the entirety of the present claims. While possibly relevant to the

technology at hand, Rognan et al. does not anticipate the present claims because it only supplies a method for predicting a single affinity, where that prediction is a structure based prediction. As noted by the claims, in the interview, and detailed below, the present claims recite that 1) two different affinity predictions must be supplied, 2) that the affinity predictions are scaled, 3) that they are combined for a final affinity prediction, and 4) that one of the two predictions must be sequence based. Rognan does not teach or suggest these elements. These are each discussed in more detail below.

First, the present claims are generally directed to a method of combining at least two different predictions of affinity in order to obtain another prediction of affinity. For example, the present claims generally include language similar to obtaining a first prediction of affinity for the peptide to a target protein and obtaining a second prediction of affinity for the same peptide to the same target protein. Thus, while Rognan could be interpreted to teach a method of determining one affinity, it does not teach the previously and currently claimed steps of determining a first and a second affinities. Moreover, the present claims also explicitly recite that the methods used to obtain the first and second affinities are different from one another. As such, Rognan does not anticipate the pending independent claims that recite the use of two different methods of determining an affinity. At best, Rognan teaches one method of determining an affinity.

Furthermore, once the results of the two different methods are obtained they are scaled or normalized by scaling. Neither Rognan nor the other cited art teaches scaling their predicted affinity. Additionally, the present claims recite that the scaled results are to be combined or summed together. Again, neither Rognan nor the other cited art is concerned with practicing two different affinities and thus cannot teach combining the scaled results together. Thus, neither Rognan nor the other cited art can anticipate the claims because the references do not teach each and every claimed element in the independent claims.

Finally, and as further clarified by the present amendment, the current independent claims also generally recite that at least one of the methods for affinity prediction employs a comparison of the sequence data to predict the affinities. As described in the specification, this technique is very different from what is taught in Rognan. While Rognan could be one of the two techniques in the presently claimed method, it does not meet this element of being a sequence based

comparison because it is a structure based technique. In light of this, Rognan does not teach this element either.

Thus, there are at least four separate elements that are in the presently recited claims that are not taught or suggested in Rognan, and Rognan cannot anticipate the present claims. As dependent claims that depend from novel claims are also novel, the remaining dependent claims are also novel over Rognan.

Claims 86, 91, 107, and 108 are nonobvious over Rognan in combination with Meister and Altuvia.

Dependent Claims 86 and 91

Claims 86 and 91 depend from Claims 85 and 90 respectively, which are novel and nonobvious for the reasons noted above. As such, Claims 86 and 91 are at least as novel and non-obvious Claims 85 and 90. As explained below, Meister and Altuvia do not overcome the deficiencies noted above in regard to the independent claims. Additionally, Claims 86 and 91 recite additional elements that further distinguish them from the cited art.

Independent Claims 107 and 108

As noted above, Rognan does not teach or suggest at least four separate elements of the currently pending claims. Meister and Altuvia do not make up for these failings, nor is there any reason for combining these references in the manner required to result in the claimed method.

The Examiner has asserted that Meister et al. teaches two algorithms based on MHC-binding motifs for predicting T cell epitopes from protein primary structure. The Examiner has further found that it would have been obvious to combine the teachings of Meister with the teachings of Rognan in order to obtain a more accurate predictive tool by incorporating both sequence and interaction data to improve particular vaccines. The Examiner has cited Altuvia, p. 246, col. 2, lines 1-7 for support of this proposed motivation in regard to combining sequence and interaction energy. Applicants respectfully traverse the rejection and disagree with the characterization of Altuvia in particular.

If anything, it appears that Altuvia may teach away from the presently claimed method (and from combining these predictions of affinity in general). The cited section of Altuvia, and

apparently Altuvia in general, is directed to a structure based approach for predicting binding affinities (*e.g.*, Altuvia concludes that the technique can be used when the "structural information about the complex is available." p. 249, col. 1, lines 2 and 3.) Indeed, the abstract of Altuvia summarizes the paper as "an approach developed to address the inverse protein folding problem" (emphasis added) and Altuvia explicitly states that sequence based techniques (such as motifs) are not involved in its technique ("[t]he computational procedure presented here succeeds in determining the MHC binding potential of peptides along a protein amino acid sequence, without relying on binding motifs." Abstract, emphasis added). Applicants respectfully note that the technique in Altuvia is not a sequence based comparison, as the tem is used in the present application, but a structure based comparison. Thus, if anything, Altuvia could be described as teaching away from the presently claimed method which recites that sequence data is not only used, but is required to determine the binding affinity. In light of this, Altuvia does not overcome the deficiencies noted above in regard to Rognan.

More importantly, Altuvia does not teach that the results of two different methods for predicting affinities should be combined, especially when one of them is a sequence based technique (as Altuvia explicitly notes that it does not use such techniques). Indeed, as Altuvia is a structure based prediction, at best, it could only motivate one to combine different structure based predictions, which is insufficient motivation to combine the sequence based prediction that is currently claimed. Moreover, Altuvia does not teach that the results from two different methods should be combined as currently recited in the claims (scaling between 1 and 0 and then combining them). As such, Altuvia does not make up for the failings of Rognan described above and their combination does not make the presently claimed method obvious.

In addition, while it may be correct that Altuvia may use a primary amino acid structure, it is only used in a structure based prediction. In particular, Altuvia is using the structure of the peptide (via pairwise contact potentials, see abstract) for it predictions. Thus, Altuvia does not teach the currently recited step of using sequence data (or sequence similarities or comparisons) to predict a binding affinity. The differences between these types of techniques are noted in the present application and understood by those of skill in the art.

Finally, Meister does not make up for the above-identified failings of Rognan and Altuvia. Meister has been asserted as teaching the analysis of primary sequences to determine a

MHC epitope. While this reference does teach the use of sequence data in predicting or determining an epitope, it does not teach or suggest that one should combine the results of two different forms of affinity prediction generally. Moreover, it does not teach that the results should be combined by scaling in the manner claimed. That is, Meister does not suggest scaling the results from 1 to 0 or combining these scaled values to obtain a result.

As none of the art teaches or suggests the presently recited elements, *e.g.*, methods of scaling the different final affinity predictions and combining the scaled results, not every element has been taught by the combination of references. Additionally, as noted above, it does not appear as though the cited reference supports the Examiner's asserted motivation to combine two different predictions of affinity. As not all of the elements have been taught by the cited art and because there is no motivation to combine the references, a *prima facie* case of obviousness has not been established.

General Comments Regarding the Art

It appears that, to some extent, the Examiner may believe that the claimed method is obvious because the idea of combining two different affinity prediction methods seems obvious. Applicants note that such logic, while perhaps appropriate for some technologies, does not apply here. First, Applicants note that affinity binding predictions are a very detailed and complicated process (as demonstrated by the art of record) in which there are many variables that are specifically and often exclusively balanced against one another.

Indeed, a general review of the references of record suggests that, in those situations where multiple techniques of prediction are taught in a single reference, it is for a comparison in order to demonstrate the superiority of one technique over another. There is no evidence that the claimed method of scaling and combining results from different techniques, in the manner claimed, has previously been thought of. In fact, it appears as though the prior art taught that various techniques are alternatives to one another rather than results that could or should be combined together in the manner claimed.

This alternative approach is appropriate if one believes that there is a single correct affinity value that is to be predicted. If such an assumption is correct, and if two different techniques provided two different answers, then one of the techniques must be "incorrect" or less

accurate. Given this, one can see that, to some extent, logic would teach away from the presently claimed method because it would be counterintuitive to combine a "correct" answer with an "incorrect" answer, thereby lowering the accuracy of the result. Applicants submit that, prior to the present application, such a dilemma would likely have prevented one of skill in the art from pursuing the claimed method. However, as noted in the present application, there are other advantages that result from practicing the claimed method.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and request the same. If, however, some issue remains that the Examiner feels can be addressed by Examiner Amendment, the Examiner is cordially invited to call the undersigned for authorization.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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